CEREBRAL HAEMORRHAGE FROM RUPTURE OF A CONGENITAL INTRA-CEREBRAL ANEURYSM IN A CHILD

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(WITH SPECIAL PLATE)

Acute cerebral vascular catastrophes in young people, and especially in children, are of infrequent incidence, and spontaneous cerebral haemorrhage as the cause is quite a rare event. Nevertheless these cases have assumed a new interest and importance, since some of them, and more especially those associated with aneurysm, have been brought within the scope of practical treatment (Dott, 1933; Dott, Hermann, and Obrador, 1937). In many cases the clinical facts do not warrant a diagnosis more exact than "acute cerebral vascular catastrophe." In children embolism and haemorrhage—from a vein in whooping-cough, purpuric states, local tuberculous and neoplastic disease; from an artery affected by aneurysm—have to be considered. If the patient survives, as indeed he does in the majority of cases, the exact nature of the responsible lesion may remain impossible of final definition (Poetzl, 1934). For example, Holden and Le Marquand (1929) report the case of a girl aged 9 in which the clinical history and findings leave no reasonable doubt that a spontaneous haemorrhage had occurred into the right frontal lobe. Absence of evidence of associated disease renders possible causes other than aneurysm extremely improbable. In adults other causes of cerebral haemorrhage, such as arteriosclerosis, increased arterial blood pressure, angiospasm (Neubuerger, 1928), vascular malformations, etc., widen the possibilities.

In the event of arterial haemorrhage from rupture of an aneurysm the bleeding may occur into the subarachnoid space or into the brain substance, or both. It may erupt into a ventricular cavity from either situation. The finding of an admixture of blood with the cerebrospinal fluid is confirmatory of haemorrhage as the cause of symptoms, but its absence does not exclude haemorrhage, which may be confined within the brain substance.

When in the case of a child spontaneous arterial haemorrhage is entirely intracerebral it may be presumed to arise from the rupture of an aneurysm situated upon one of the smaller intracerebral arterial branches. Mallen's case (1933) was one of fatal cerebral haemorrhage. The patient was a 9-year-old girl who, without previous illness or injury, suddenly collapsed while drinking tea. The clinical features suggested cerebral haemorrhage. Death occurred a few hours later. At the post-mortem examination the clot was found in the right temporal lobe. The author attributed the haemorrhage to the rupture of an aneurysm, although the presumed aneurysm could not be identified.

There are probably several reasons why only a few examples of intracerebral aneurysm are on record. Aneurysms are certainly of less frequent incidence on the smaller arteries within the brain substance than on the larger vessels upon its base. They are also more difficult to find, since they are necessarily of small size. The delicate wall of the sac tends to collapse when the blood pressure falls at death, and to shrink still more if the specimen is subjected to artificial fixation. When rupture of the aneurysm is the cause of death the difficulties are further increased, for the minute lesion is embedded in surrounding clot, and as it contains clot itself it is rendered extremely inconspicuous.

Aetiology

Aneurysms of the cerebral arteries may be congenital, arteriosclerotic, or mycotic. It is now recognized that the majority of them are congenital. The researches of Forbus (1930) drew attention to the embryological basis of these lesions in developmental defects of the muscular coats of arteries at the joining of trunk and branch. Arteriosclerotic aneurysms have rarely been found in the brain substance. Green (1930) records two cases of rupture of such lesions with associated intracerebral haemorrhage. Arteriosclerotic lesions, however, affecting elderly subjects do not come within the scope of this paper. Mycotic aneurysms are rare in children, and we have been unable to find any record of intracerebral haemorrhage associated with this type.

Gull (1858) records an instance (second case) of a small aneurysm in the substance of the pons which ruptured and caused haemorrhage into the surrounding tissues. In this case arteriosclerosis of the basilar trunk was noted and contracted kidneys were present. No histological record of the sac or affected vessel is given, so that it cannot be decided whether the lesion was degenerative, mycotic, or congenital in origin. It is of interest to note Gull's remark: "Though intracranial aneurysms usually occur on the larger trunks of the vessels as they lie at the base of the brain or in the fissures between its lobes, the smaller branches, after entering the cerebral substance, are not exempt." Charcot and Bouchard (1868) described multiple dilatations of the intracerebral arteries in elderly arteriosclerotic patients who had died from apoplexy. It is now considered doubtful if these appearances represented actual aneurysms.

We have been unable to find a record in the literature of an instance of a verified congenital intracerebral aneurysm, with or without rupture and haemorrhage.

Case Record

A male child aged 4½ years was admitted to the Royal Edinburgh Hospital for Sick Children in an unconscious state on April 23, 1937. His parents were healthy people, and in particular there was no evidence to suggest parental syphilis. He was an only child. He had enjoyed excellent health with the exception of an uncomplicated attack of whooping-cough at the age of 3. The only explanation which the parents could suggest for his sudden illness was that he might have "headed" the ball with which he was playing at the time of onset of his symptoms. The ball was actually a light rubber toy, and could not possibly have inflicted a percussional injury to the head. The cerebral haemorrhage which he suffered from was apparently spontaneous in character. His playing was quite active, and no doubt was associated with a physiological rise in arterial blood pressure. The child interrupted his play spontaneously and abruptly, sat down, and complained that his left ear was painful. Presently he collapsed and "seemed to shake." His right eye was observed to turn outwards. It was realized that he was unconscious.

CLINICAL HISTORY

On admission to hospital shortly afterwards he was still unconscious, but he resisted physical disturbance and would attempt to push the doctor's hand away. His complexion was healthy, the pulse rate was 60, respirations 20, and temperature 97° F. Moderate neck rigidity was present and Kernig's sign was positive on the left side. There was no strabismus;

the pupils were moderately dilated and equal. The Babinski sign was positive on both sides. When stimulated by touch in any part of the body the legs were drawn up, this movement being weaker on the right side, and the child would roll over on to that side. Lumbar puncture yielded blood-stained fluid under greatly increased pressure.

Shortly after admission to hospital breathing ceased; the pulse remained of good quality. A tracheal tube was inserted and artificial respiration was effectively maintained. Exploratory cranial perforations were made in each parietal region. No collection of blood was found on the brain surface. The brain was very tense. On each side a cannula was directed through the brain towards the lateral ventricle. When the ventricular cavity was entered fluid blood, with fragments of clot and disorganized cerebral tissue, escaped from the cannula on each side. From this it was surmised that a massive intracerebral haemorrhage had occurred and had ruptured into one of the ventricular cavities. It was apparent that severe damage to the brain substance had been sustained. No further active treatment was attempted. Artificial respiration was continued and the circulation remained satisfactory for a further period of three hours. Progressive circulatory failure then ensued. No natural respiratory movements occurred. The child died fifteen hours after the onset of the symptoms.

NECROPSY

Post-mortem examination was limited to the head. No abnormality of the brain surface was noted. During removal of the brain a large quantity of blood escaped from its interior through an accidental tear which opened a blood-containing cavity in the left frontal lobe. After suitable fixation the interior of the brain was examined. An extensive haemorrhage had occurred into the substance of the left frontal lobe. A cavity filled with blood clot had been formed. It was of irregular shape, about 4 cm. in diameter, and was situated immediately anterior and lateral to the anterior horn of the lateral ventricle (Plate, Figs. 1 and 2). It extended laterally to within a few millimetres of the brain surface, and its inner wall was about 2 cm. from the mesial surface of the brain. The cavity had ruptured into the adjacent ventricle, and the entire ventricular system was filled with blood clot in which disorganized cerebral tissue was mixed.

From the clinical features of the case aneurysm was suspected as the underlying cause of the spontaneous haemorrhage. On careful inspection of the haemorrhagic cavity in the brain a ruptured aneurysm was found embedded in the anterior part of its medial wall. The fundus of the sac projected into the cavity. The rupture had occurred at this point, and the clot within the cavity was adherent to the tear in the sac and was continuous with the clot within its lumen. The aneurysm was of oval form and measured about 6 mm. in its longest diameter. The wall appeared relatively thick and fibrous except at the fundus, where rupture had occurred; it was attenuated at this part. The sac took origin from a bifurcation of one of the deep branches of the anterior cerebral artery within the brain substance and about 2 cm. deep to the mesial surface of the frontal lobe.

About 1 cm. posterior to this aneurysm a second smaller aneurysm was found. It had not ruptured. The small artery on which it was situated had been exposed in about 1 cm. of its course by the destruction of the brain substance around it occasioned by the haemorrhage. Its distal end had evidently been torn across by this disruptive agency. The vessel thus lay exposed upon the wall of the haemorrhagic cavity. About the middle of its exposed portion, and at the point of origin of a minute branch, an aneurysmal sac about 1.5 mm. in diameter was found.

The smaller, unruptured aneurysm was noted on microscopical examination to constitute a saccular dilatation, communicating by a relatively wide neck with the lumen of the parent artery (Fig. 3). The relation of the neck of the aneurysm to the origin of a small arterial branch was verified by serial sections. The muscle tissue of the coat of the parent artery ended abruptly at the neck of the sac. Elastic fibres were traceable in the sac wall for a short distance beyond this point, not as a properly formed elastic lamina but only as separated strands. Beyond this they were no longer apparent, and the greater part of the sac wall contained neither muscle nor elastic fibres. It was composed of fibrous tissue derived from the tunica intima, which was greatly thickened round the neck of the sac and round half its circumference on one side only. The remainder of the wall, corresponding to a somewhat asymmetrical fundus, was notably attenuated. There were no atheromatous degenerative changes, nor was there any evidence of inflammatory reaction. The wall of the artery proximal to the aneurysm showed no sign of disease. The sac contained a recent thrombus—no doubt the consequence of the rupture of the artery distal to the aneurysm and arrest of blood flow through the vessel.

The microscopical section of the larger aneurysm which had ruptured cut the sac near the fundus, close to the place of rupture, and it included surrounding brain substance and the wall of the cavity formed by the haemorrhage. The structure of the sac was similar to that of the smaller lesion just described. The sac wall was very thick over its greater part and except where the fundus projected into the haemorrhagic cavity. Here it was very thin, and at this spot rupture had occurred. Again the parent artery showed no sign of degenerative or inflammatory disease; and again the aneurysmal sac contained clot, the thrombotic process having no doubt spread to its interior through the rupture aperture from the clot which formed around it in the extravasated blood. The brain substance immediately surrounding the sac was infiltrated by collections of macrophages which were heavily loaded with haemosiderin. These cells could be traced in perivascular spaces to some distance from the aneurysm. The wall of the haemorrhagic cavity showed only recently extravasated blood.

It is evident from these observations that haemorrhage from the aneurysm had occurred at a date considerably earlier than that of the fatal rupture. It is to be supposed that there was only a limited leakage of blood at that time, since no clinical history suggestive of an earlier "cerebral catastrophe" could be elicited. It is probable that at least part of the great fibrous thickening which affected the major portion of the sac wall was the result of organization of this earlier blood clot around the sac. The fibrous tissue of the sac wall being mature and relatively acellular, these events were probably of long standing.

Several portions of the larger superficial cerebral arteries from the base of the brain and elsewhere were examined for congenital defects of their muscular coats. Two such defects were found in relation to the junction of branches of the anterior perforating group with the left middle cerebral artery. The defects were similar to those described by Forbus. They were at the acute angle of the junction in each case: there was a gap in the muscular coat, which was filled by fibrous tissue continuous with that of the adventitia. The internal elastic lamina was intact and the tunica intima was unaltered (Fig. 4). Except for these microscopical defects at the branch junction lines the structure of the vessels was normal.

Discussion

There can be no doubt that the aneurysms in this case were of developmental origin. There was no evidence from the clinical history, or from the microscopical examination of the aneurysmal sacs, associated arteries, and other cerebral arteries, of degenerative or inflammatory disease of the surrounding vessels. On the contrary, the histopathological findings are in all respects characteristic of congenital aneurysmal lesions. The relation of the aneurysms to blood-vessel junctions is consistent with this developmental origin. The age of the patient and the demonstration of "Forbus defects" in other arteries at the base of the brain complete the convincing evidence

of their developmental origin. Forbus has shown that the minute defects in the muscular coats of arteries which are frequently found at vessel junctions may be regarded as potential aneurysms. Whether such a defect develops into an actual aneurysmal saccular protrusion or not depends on the extent of the defect and conditions of blood pressure to which it is subjected. Whether such an aneurysm ruptures or not depends similarly on the blood pressure to which its wall is subjected and to the resistance of that wall. Probably the size of the original defect has an influence on the thickness and resistance of the wall of the saccular protrusion.

Although we are unable to find any preceding record of a congenital aneurysm situated within the brain substance, and although these lesions are doubtless much more often associated with the larger arteries at the base of the brain or in its principal fissures, our record demonstrates that such a lesion may occur. For the reasons mentioned above the incidence may be more frequent than the absence of recorded cases would suggest. A congenital intracerebral aneurysm is, moreover, a possible cause of apoplexy to be reckoned with even in the case of a young child.

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DEATH FROM QUININE POISONING

BY

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(WITH SPECIAL PLATE)

Since fatal blackwater fever is rare in Great Britain the following description of a case in which death occurred from a complaint almost indistinguishable from the most severe form of blackwater fever may be interesting. This patient had neither suffered from malaria nor left England.

Quinine is used in all parts of the world, and for many reasons. Its minor toxic effects, as in cinchonism, are well known; the occurrence of urticarial rashes after small doses—a true allergic response—is not uncommon, but if the drug is used in moderate doses fatal results are rare, except in the case of malarial patients who develop blackwater fever. Fairley (1937; Fairley and Bromfield, 1934, 1937) has brought forward evidence which demonstrates that blackwater fever can occur in patients who have received no anti-malarial treatment for many months.

History of Case

The patient, a married woman aged 34, had always lived in or near London, and had never left England. She had never suffered from malaria or any illness resembling malaria. She had had four previous pregnancies—two had miscarried and two had gone to term. A week before admission a specialist confirmed her fear that she had again become pregnant. The day before admission she bought a box of pills, and swallowed sixteen of them some time after noon, leaving one in the box. Analysis later demonstrated that the remaining pill, weighing 0.67 gramme, contained 0.38 gramme of quinine sulphate: it seems probable, therefore, that she took a total of 6.08 grammes of quinine sulphate, or 5.04 grammes (76 grains) of the pure alkaloid. On the same evening she was taken ill with headache, vomiting, pyrexia, and increased pulse rate; there was abdominal pain and vaginal bleeding. Her husband found her in this condition and sent for her physician, who at once had her removed to hospital. His note stated: "Called at 11.15 p.m. Temperature 102°, pulse 132. Headache, vomiting; scarlet rash all over body, abdominal pain, vaginal haemorrhage, all said to have been present for many hours. No history of contact with scarlet fever, and no signs of scarlet fever."

CLINICAL FINDINGS

On admission at 2 a.m. her temperature was 102.6°, pulse 140, respirations 40. She was restless and clearly in pain, and there was a suggestion of a urine-like smell about her. The whole body was covered with a uniform copper-coloured rash. It did not fade on pressure. The conjunctivae showed an icteric tinge. The mucous membranes were a good colour and the tongue was quite clear and moist. No sign of activity was detected in the breasts. The abdomen was full and was tender all over, particularly in the lower half. Here the fundus of the uterus was palpable. In the vagina inspissated and curiously altered blood was found. This was offensive. The cervix was patulous, and the uterus was enlarged to the size of a ten-weeks gestation and was tender. No other tumour was palpable. There was slight oedema of the legs. Two ounces of urine was withdrawn by means of a catheter. This urine was black.

INVESTIGATIONS

There were signs of pregnancy complicated by abortion, but whether the miscarriage had just occurred or was about to occur was not clear. Tenderness and rigidity were noted in the abdomen, suggesting peritonitis. Finally there was the remarkable colour. In artificial light its hue was not easily decided, and it was thought by one to be icteric, by another to be that caused by prontosil soluble, by a third to be that of a *Clostridium welchii* septicaemia. The possibility of some drug idiosyncrasy remained.

The urine was almost black, and its centrifuged deposit showed nothing but masses of amorphous yellow deposit and a slightly excessive number of white blood cells; a Gram film revealed no micro-organisms. When daylight arrived it became clear that the colour was not that of jaundice or of prontosil soluble, but a vivid, rather coppery, mahogany brown, resembling that occurring in *Cl. welchii* septicaemia; the probability of this infection being the cause of the colour was, however, slight, since none had been found in the urine, nor was the patient ill enough. The urine was found to contain methaemoglobin in very high concentration, all four bands of which became visible when a 1 cm. layer of urine diluted to 1 in 20 was examined with the pocket spectroscope.

A specimen of blood was next examined. Aerobic and anaerobic cultures were taken, and these proved sterile; the blood, allowed to clot and then centrifuged, set free serum so dark that the surface separating clot and serum was indistinguishable in daylight. Spectroscopic examination of the serum showed a band in the red at 630 mμ; the blood urea was 128 mg. per 100 c.cm.; the direct van den Bergh reaction was positive in fifteen seconds, and the total bilirubin was 78 units, or 39 mg. per 100 c.cm. The serum phosphatase was 14.4 units by the method of King and Armstrong (normal 4 to 14 units).

Further investigations were made at intervals to confirm the diagnosis and prognosis, with the following results: Second day after admission: red cells, 3.2 millions; leucocytes, 26,800. Third day: red cells, 1.85 millions; leucocytes, 29,800. Fifth day: band in red still present in serum but very weak; blood urea, 325 mg. per 100 c.cm.; alkali

KATE HERMANN AND AGNES McGREGOR: CEREBRAL HAEMORRHAGE FROM RUPTURE OF A CONGENITAL INTRACEREBRAL ANEURYSM IN A CHILD

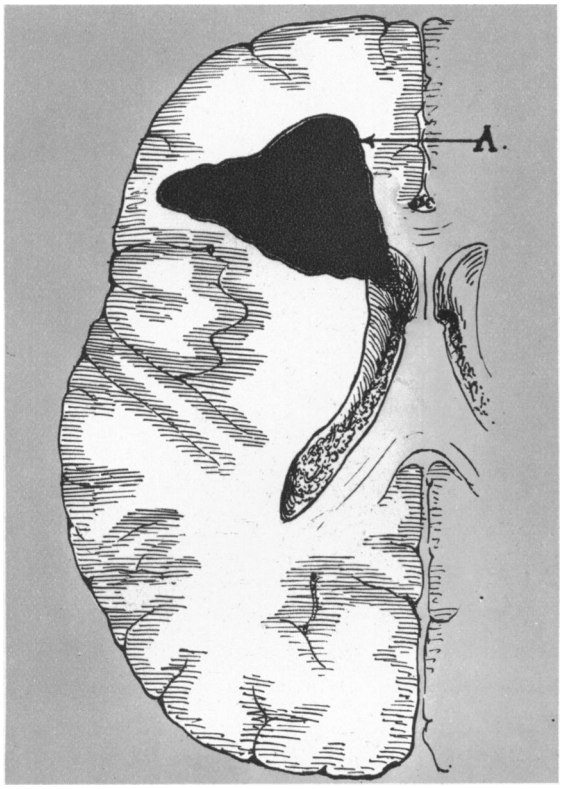

FIG. 1.—Diagrammatic drawing of left cerebral hemisphere, showing position of ruptured aneurysm, A, and of surrounding haemorrhage.

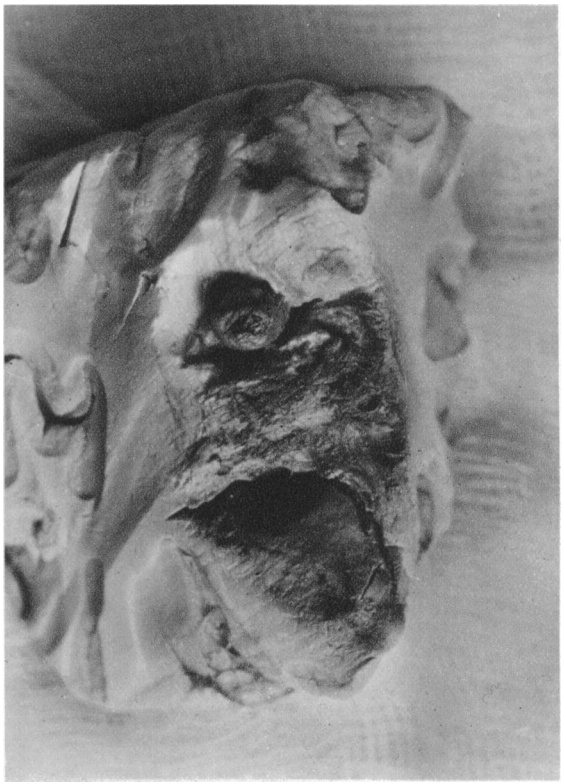

FIG. 2.—Photograph of left frontal lobe (1¼ times natural size), showing part of cavity formed by haemorrhage and ruptured aneurysm projecting upon its medial wall.

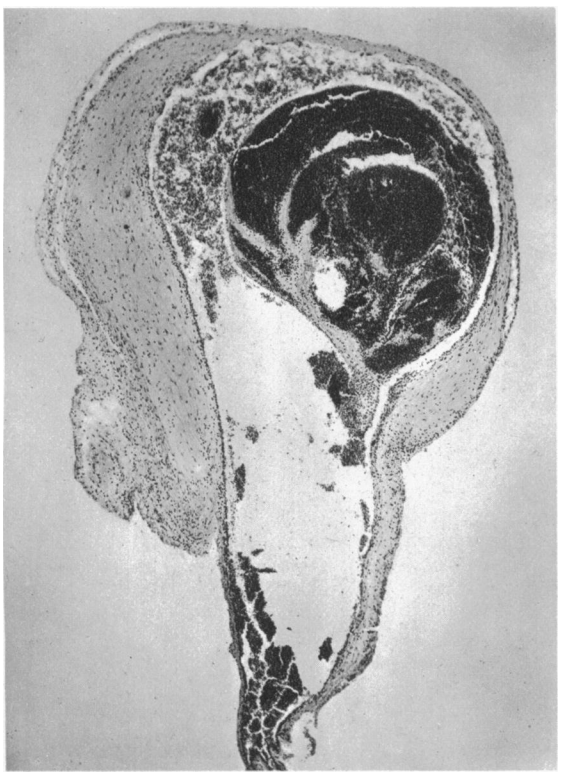

FIG. 3.—Photomicrograph of smaller unruptured aneurysm (× 30). Note fibrous sac wall, devoid of muscle and elastic fibres, thickened tunica intima at sides, and extreme attenuation at fundus.

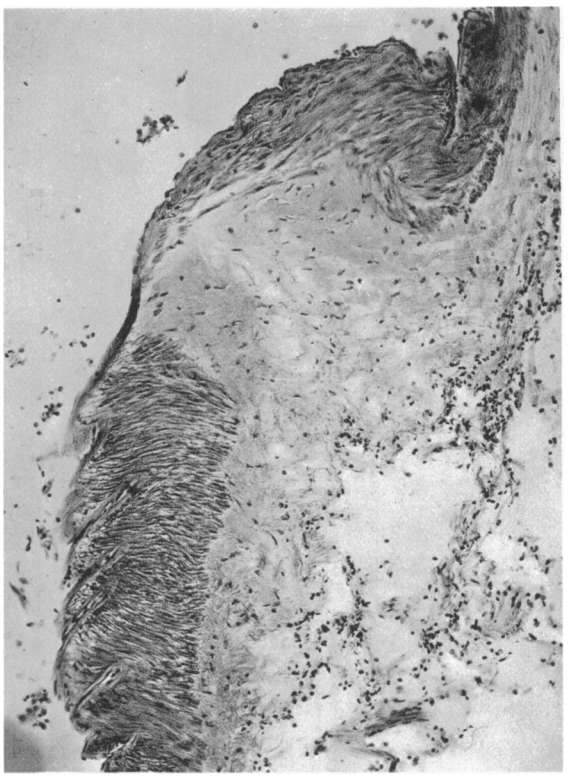

FIG. 4.—Photomicrograph (× 100) of congenital defect in muscular coat at origin of anterior perforating branch from middle cerebral artery. Note gap in muscular coat filled with fibrous tissue continuous with that of adventitious coat. Internal elastic lamina is intact and tunica intima normal.